

Abstract of the Disclosure

Provided herein are methods for identifying the presence or absence of a polypeptide variance between different biological samples and corresponding methods for generating a high-throughput screen to rapidly identify variances of one or more polypeptides in different biological samples. In particular, a variance in a post-translational modification on a particular polypeptide in the biological samples can be identified, such as the presence or absence of a polypeptide having an attached phosphoryl moiety, for example. In these methods, a catalytically inactivated enzyme (*i.e.* bindingzyme) is utilized as a substrate-specific binding protein. These bindingzymes can bind to one or more substrates in biological samples and a bound substrate can act as a marker to distinguish one sample from another. These methods also are useful for isolating substrates for their identification, for the detection of substrates in a sample, and for the discovery and development of ethical drugs.